REMARKS

The Office Action mailed October 3, 2000, has been received and reviewed. Claims 25-29 are currently pending in the application. Claims 25-29 stand rejected. Claims 30-34 have been added. Support for the step-gradient waveguide of claims 30-34 can be found on page 5, line 1 and throughout the specification. The application is to be amended as previously set forth. All amendments are made without prejudice or disclaimer. Applicant respectfully requests reconsideration of the application as amended herein and in view of the arguments below.

I. Drawings

The drawings were objected to by the Examiner under 37 CFR § 1.84. Upon notice of allowance, formal drawings will be submitted.

II. 35 U.S.C. § 112, Second Paragraph

Claims 28 and 29 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Claim 28 was rejected as assertedly being vague and unclear as to whether the oligonucleotide primer is the capture molecule of claim 25 or is used in addition to the capture molecule of claim 25. Applicants have amended claim 28 to include the phrase "wherein an oligonucleotide primer acting as a capture oligonucleotide complementary to said analyte is immobilized". This should clear up any possible confusion relating to the oligonucleotide primer. Additionally, "biofin" has been corrected to its proper spelling "biotin". Therefore, applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, second paragraph rejection to claim 28.

Claim 29 was also rejected for allegedly being vague. Specifically, the Office Action was confused as to the recitation of "another sequence of the analyte". Applicants have amended the claim to recite "a second sequence of the analyte" to clear up any possible confusion contained in the claim.

III. 35 U.S.C. § 102(b) Anticipation Rejections

A. Claims 25-27 and 29 Rejections by Herron

Claims 25-27 and 29 were rejected under 35 U.S.C. § 102(b) as being anticipated by Herron et al. ("Fluorescent Immunosensors Using Planar Waveguides", SPIE, 1885: 28-39 (1993)). Applicants respectfully traverse this rejection as set forth below.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). In the present case, the cited art fails to disclose the subject matter contained in the amended claims of the present invention.

Specifically, Herron et al. only discloses an immunosensor for the detection of chorionic gonadotropin. Additionally, Herron et al. state that the requirement of two monoclonal antibodies that bind to the well separated regions of the analyte "limits the classes of analytes that the sandwich assay can detect to macromolecules such as proteins and polysaccharides." Claim 25, as amended, recites an assay comprising a "plurality of capture oligonucleotides site-specifically immobilized thereon, wherein said capture oligonucleotides have a binding site which selectively binds a selected analyte". Therefore, amended claim 25 is not anticipated by Herron et al., as it discloses an assay that is capable of detecting smaller molecules, such as oligonucleotides, that bind to their corresponding nucleotide as opposed to the macromolecules disclosed by Herron et al..

Thus, independent claim 25, as amended, is not anticipated by Herron et al.. Accordingly, it is respectfully submitted that the presently amended independent claim 25 is allowable under 35 U.S.C. § 102(b).

In addition, claims 26-27 and 29, which respectively depend from independent claim 25, are each allowable, among other reasons, as depending from claim 25, which is allowable.

B. Claims 25-26 and 29 Rejections by Hirschfeld et al.

Claims 25-26 and 29 were rejected under 35 U.S.C. § 102(b) as being anticipated by Hirschfeld et al. (U.S. Patent 4,558,014). Applicants respectfully traverse this rejection.

Hirschfeld et al. disclose an assay apparatus including a sensor in which the light is evanescently coupled back into the waveguide. (*See*, Col. 4, lines 20-23 and Col. 13, lines 15-41.) Independent claim 25 of the present invention, as amended, claims an assay comprising the element, "providing detection means operably disposed for detecting fluorescence emitted from the waveguide". Thus, the light in the claims of the present invention is actually emitted from the waveguide as opposed to evanescently coupling back into the waveguide as is seen in Hirschfeld et al. Therefore, amended independent claim 25 of the present invention is not anticipated by Hirschfeld et al. because Hirschfeld et al fail to teach each and every element contained in the claim 25 of the present invention.

In addition, claims 26 and 29, which respectively depend from independent claim 25 are each allowable, among other reasons, as depending from claim 25, which is allowable.

Accordingly, reconsideration and withdrawal of the rejections under U.S.C. 102(b) to claims 25-26 and 29 is respectfully requested.

IV. 35 U.S.C. § 103(a) Obviousness Rejections

Claim 28 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Herron et al. and Hirschfeld et al. Applicants submit that Herron et al. and Hirschfeld et al. do not teach or suggest the invention as claimed in claim 28.

The Office Action provides that Herron et al. and Hirschfeld et al. allegedly teach all of the elements of the present invention except for the use of an oligonucleotide primer reagent for detection of a nucleic acid analyte as set forth in claim 28. The Office Action states that it would have been obvious to one of ordinary skill in the art to use an oligonucleotide primer reagent in the methods of Herron et al. and Hirschfeld et al.

Applicants submit that the instant invention is not taught or suggested in the prior art. Applicants further submit that, to establish a *prima facie* case of obviousness under 35 U.S.C. § 103(a), three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the cited prior art reference must teach or suggest all of the claim

limitations. Furthermore, the suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicants' disclosure.

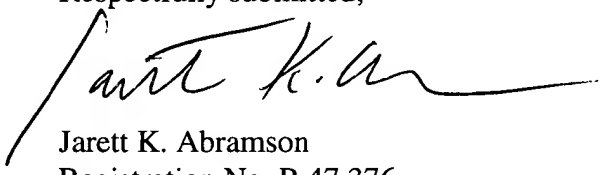
Applicants point out that claim 28, as amended, teaches an "immunofluorescence assay according to Claim 25, wherein an oligonucleotide primer acting as a capture molecule complementary to said analyte is immobilized to said step-gradient waveguide by amine-reactive, thiol-reactive, or (strep) avidin-biotin coupling chemistry." Specifically this claim discusses immobilization chemistry rather than the type of assay being performed. Moreover, there is no reason to assume a priori that oligonucleotides can be optimally immobilized using the same methods as used for immobilizing antibodies. In fact, one skilled in the art would not assume that the two types of capture molecules could be immobilized using the same methods. This is why the applicants performed the experiment with oligonucleotides and included examples to that effect in the teachings.

Accordingly, reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejection to claim 28 is respectfully requested.

CONCLUSION

In view of the amendments and remarks presented herein, applicants respectfully submit that the amended claims define patentable subject matter. If questions should remain after consideration of the foregoing, the Examiner is kindly requested to contact applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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Encl: Version with markings to show changes made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please replace the first paragraph on page 25 with the following:

The transcriptional promoter site of the T3 RNA polymerase is employed as a model oligonucleotide sequence in these studies. The T3 promoter is a 20-mer consisting of the following sequence: 5' AATTAACCCTCACTAAAGGG 3' (SEQ. ID. NO. 1). This oligonucleotide is synthesized and purified by a molecular biology service facility at the University of Utah. When used in DNA hybridization assays, it is immobilized to waveguides (using procedures described below) and used as the "capture" oligonucleotide. It is also used as the soluble inhibitor in competition assays. A second oligonucleotide sequence, complementary in sequence to the T3 promoter, is synthesized at the same service facility, fluorescently-labeled and used as the soluble "tracer" oligonucleotide in DNA hybridization assays. To this end, the oligonucleotide is synthesized with a terminal amino group on the 3' end and labeled with Cy-5 (Molecular Detection Systems, Pittsburgh), a red-emitting fluorescent dye.

Please replace the second full paragraph on page 28 that carries over to page 29 with the following:

Assay I is a direct binding assay between two complementary oligonucleotides. The T3 RNA polymerase promoter site was chosen as a model system for our feasibility studies. The T3 promoter is a region spanning 20 bases with the following sequence: 5' AATTAACCCTCACTAAAGGG 3' (SEQ. ID. NO. 1). An oligonucleotide (T3 promoter) with this sequence was synthesized, biotinylated at the 5′ end (via a spacer) and immobilized to waveguides (silica or polystyrene) coated with either avidin or stepavidin. A second nucleotide with a complementary sequence (anti Te) was also synthesized and labeled with Cy-5, a red-emitting fluorescent dye. Solutions with increasing tracer concentration were exposed to the waveguide and the fluorescence of bound tracer was plotted versus soluble tracer concentration. Assay II is a competitive binding assay in which unlabeled Anti T3 competes with Cy-5 labeled Anti T3 for binding to immobilized T3 promoter. In this case different concentrations of unlabeled Anti T3 were mixed with a fixed concentration of labeled Anti

T3 (tracer). The fluorescence of bound tracer was measured for each mixture and plotted versus unlabeled Anti T3 concentration.

Please replace the footnote under Table 2 on page 29 with the following:

†Abbreviations: Cy-5, an amino-reactive red-emitting fluorescent dye produced by Biological Detection Systems (Pittsburgh, PA); T3 Promoter, the transcriptional promoter site of T3 RNA polymerase which consists of the sequence 5' AATTAACCCTCACTAAAGGG 3' (SEQ. ID. NO. 1); Anti T3, oligonucleotide with a complementary sequence to the T3 promoter.

IN THE CLAIMS:

A marked up version of each of the presently amended claims, highlighting the changes thereto, follows:

25. (Amended) [An immunofluorescence] A fluorescence assay, comprising the steps of:

providing a waveguide which is optically conductive and which has at least one surface having a plurality of capture [molecules] oligonucleotides site-specifically immobilized thereon, wherein said capture [molecules] oligonucleotides [having] have a binding site which selectively binds a selected analyte;

providing a light source operable to emit a light beam in a desired wavelength range and positioned to send light into the waveguide;

providing detection means operably disposed for detecting fluorescence emitted from the [biosensor] waveguide;

providing a sample comprising a buffer and a plurality of molecules of a selected analyte;

providing a plurality of tracer molecules which are operable to emit fluorescence in response to stimulation by light from the light source;

combining the sample with the tracer molecules to produce a test solution;

placing the test solution in contact with the waveguide surface while operating said light source to direct light into the waveguide; and

selectively detecting fluorescent light emitted from the tracer molecules.

26. (Amended) The assay of Claim 25, wherein said step of providing a waveguide with site-specifically immobilized capture [molecules] oligonucleotides includes the steps of:

coating the waveguide surface with a first coating to produce a coated surface;

providing a plurality of capture [molecules] oligonucleotides;

modifying a single moiety which is the same on each capture molecule, to produce activated capture [molecules] oligonucleotides having a modified moiety constructed to be coupled to the first coating; and

treating the coated surface with the activated capture [molecules] oligonucleotides under conditions to cause the modified moiety to couple to the first coating and thereby immobilize the activated capture [molecules] oligonucleotides to the waveguide surface.

27. (Amended) The assay of Claim 25, wherein said first coating is selected from the group consisting of: avidin, biotin, a hydrogel formed of polymethacryloyl polymers, and a modified polyethylene glycol.

28. (Amended) The [immunofluorescence] assay [according to] of Claim 25, wherein an oligonucleotide primer[,] acting as a capture oligonucleotide complementary to said analyte is immobilized to said waveguide by amine-reactive, thiol-reactive, or (strep) [avidin-biofin] avidin-biotin coupling chemistry.

29. (Amended) The [immunofluorescence] assay [according to] of Claim 25, wherein said tracer molecules are complementary to [another] a second sequence of said analyte.

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